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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful – the editor, alone, is responsible for their type, their tone and their tenor.

AGAIN! AND AGAIN!!

AS IF staged, in point of time and type, a series of medical mishaps have occurred during the past few months which definitely emphasize the value of the recently enacted legislation for the control of food, drugs and cosmetics.

One case in point was the famous and fatal sulfanilamide experience, where a hundred persons met death through the dispensing of a toxic combination of this new antiseptic in an *unstudied* organic solvent.

Then there was the case of a cancer serum originating in a *seemingly* well-controlled medical laboratory associated with a Philadelphia scientific institute. This toxic serum also caused many deaths.

Now comes a third such episode, which might have had disastrous results except for the alertness of a consulting pharmaceutical chemist who detected the mistake and reported his findings to the State Board of Pharmacy.

The Commonwealth of Pennsylvania, through its State Board of Pharmacy Laboratory, has recently issued the following release, and it speaks for itself. Note that in this, as in the other instances, these were not errors of well-organized, well-managed and well-established pharmaceutical houses. Had it been so, I am quite certain that we should have known more of it, through the medium of the screen, or from medical headquarters.

This is the release:

"Pharmacists are hereby warned that any 'Bad-Ex Salt' received by them subsequent to October 20, 1938, may be poisonously adulterated with antimony. No control numbers or marks appear on the package so that the only way to determine if a package is adulterated is to test it chemically for antimony. Pharmacists are requested to recall any samples of 'Bad-Ex' which may be adulterated and send them to the State Board of Pharmacy Laboratory, 114 Walnut Street, Harrisburg, Pa.

On December 22, Joseph F. McDonnell, Jr., Chief Chemist for the State Board of Pharmacy was informed by Dr. J. W. E. Har-

risson of the firm of LaWall and Harrisson, analytical chemists of Philadelphia, that antimony had been found in a sample of 'Bad-Ex' an effervescent salt supposedly containing Sodium Sulphate, Sodium Bicarbonate, Sodium, Chloride, and Tartaric Acid. This sample had been sent to him by an agent of the Pennsylvania Department of Agriculture. Dr. Harrisson at the same time notified the U. S. Food and Drug Administration.

The preparation 'Bad-Ex' was labeled as prepared in Philadelphia by the American Laboratories but upon checking the address it was found that the firm had moved away some years previously. A check of wholesalers' records disclosed that orders were being sent to an Adco Works, Carlisle, Pa. It developed that this is a firm making a patent fertilizer material and owned by Dr. Fred M. Lawrence, a physician of Carlisle.

Dr. Lawrence made the 'Bad-Ex' salt, with the assistance of his wife and a boy helper, at his residence, 333 W. High Street, Carlisle. The 'laboratories' consisted of a room in the cellar and the equipment, one old balance.

The adulteration was brought about when a 25-pound container plainly marked as antimony and potassium tartrate was used to compound the preparation instead of tartaric acid, in the amount of approximately 10 per cent. A manufacturer's invoice purporting to be the one for this shipment reads 'tartaric acid.' (Italics ours.)

The Laboratory of the State Board of Pharmacy under Chief Chemist McDonnell, has already tested over 310 samples of 'Bad-Ex' in connection with this case in a check-up as to the number of adulterated packages outstanding.

This entire episode indicates the necessity for the pharmaceutical profession to insist on new legislation leading to a strict annual licensing of manufacturers and distributors of drugs and technical poisons, and the restriction of the retail distribution of these potentially dangerous products to registered pharmacies in the interest of the public welfare."

—with which we thoroughly agree.

IVOR GRIFFITH.

ORIGINAL ARTICLES

THE COMPARATIVE PHYSIOLOGICAL ACTION OF BENZEDRINE (AMPHETAMINE) AND DERIVATIVES ON DAPHNIA MAGNA[1, 2]

By Arno Viehoever and Isadore Cohen

Philadelphia College of Pharmacy and Science

THE experimental methods employed in drug evaluation and standardization using *Daphnia magna* have been reported by Viehoever and his associates (1-17, 20, 21) and by Tinsley (18, 19). The transparency of *Daphnia magna* permits, without any surgical procedure, the intimate observation of the muscular, nervous, circulatory, digestive, and glandular systems. Thus the effects which the active substance may produce upon the internal functions can be seen directly.

Daphnia which are standardized in respect to age, sex, nutritional and environmental histories offer excellent material for quantitative studies. The rate of heart beat and respiratory movements are constant for a given age group at a definite temperature. Thus, alterations + or — of the normal rate in these functions can be quantitatively expressed.

The swimming action of normal daphnia is so characteristic that any impairment to it may be considered an important toxic symptom. Abnormality in swimming combined with internal symptoms has been studied in such detail, that a quantitative estimation of the degree of debility of the test animal can be arrived at without recourse to the use of death as the only reference point for comparison (7).

Substances to be tested are administered in solution or suspension in the culture medium or directly by micro-injection. The accumulative effects of a test substance in low concentrations can be readily studied for several days, and observations made as to the further growth of the animal, effect on reproduction, etc.

[1] Contribution from the Gross Laboratory for Biological and Biochemical Research.

[2] Test substances supplied to us by Smith, Kline & French Laboratories.

It has been our policy to test as many representative classes of active agents as possible upon *Daphnia magna* for the purpose of comparing the vertebrate and invertebrate responses to the same substance. We present in this contribution some of our observations of the comparative effects of Benzedrine sulfate, Paredrine hydrobromide and Paredrinol sulfate upon *Daphnia magna.*

Response of Daphnia Magna to Benzedrine Sulfate (Amphetamine Sulfate)

0.1% concentration in culture water

Five animals were observed in one chamber of the comparoscope. Five were used as controls.

Observations

After 3 min. Onset of convulsions, eye muscles are relaxed or paralyzed, a precipitate drop in heartbeat rate and constrictions in midgut are noted. Animals come to surface with steady beat of antennae, swim on back or turn over sidewise with shell distended.

After 10 min. Convulsions are weaker, but beat of antennae is steady, long rest periods for those sinking to bottom are noted.

After 15 min. No marked change.

After 28 min. Very long rest periods.

After 50 min. Heartbeat rate is depressed to about 100/min., respiratory movements are slow and feeble, eye muscles and gut still paralzed (partial evacuation).

After 1 hour. Returned to culture water.

After 2 hours. Appear to be recovering.

Next day. Recovery is complete.

After 21 hours. 15 other daphnia (not returned to culture) are all dead.

Using the tentative A. O. A. C. daphnia method for laxative assay (11), Benzedrine sulfate at this concentration possesses some laxative properties.

0.01% concentration in culture water

Five animals were observed in Vie-tubes as in the tentative A. O. A. C. daphnia method for laxative assay. The results after 20-25 minutes were:

1- 50% evacuation.
2- 75% evacuation.
3-100% evacuation.

The eye muscles and intestine were not paralyzed, while the heartbeat rate and the respiratory movements were not as depressed as in the higher concentrations. As expected, the intensity of reaction is not as great in the same time units as in the higher concentration of Benzedrine sulfate.

Effect of Benzedrine Sulfate in Lower Concentrations:

0.01%, 0.005%, 0.002%, 0.001%

Ten daphnia were placed in museum jars containing 100 cc. of the above solutions.

Drug effect is visible in 7 minutes at 0.01% (convulsions).

Drug effect is visible in 13 minutes at 0.005% (convulsions).

No drug effect is visible in 1 hour in 0.002% and 0.001%.

0.01% concentration in culture water

After 47 min. Complete evacuation, eye muscles are not affected, the heartbeat rate 150-180/min. (normal 280-300), respiratory movements are slowed.

After 3 hours. Convulsions continue.

0.005% concentration in culture water

After 13 min. Heartbeat rate is 200/min., respiratory movements are slightly depressed.

After 2 hours. Heartbeat rate is 160/min., respiratory movements are further depressed, complete evacuation.

0.002% concentration in culture water

After 3 hours. Heartbeat rate is slightly lowered (250/min.), respiratory movements are correspondingly slower, 75-100% evacuation.

0.001% concentration in culture water

After 3 hours. Animals are normal, 5-50% evacuation.

In all concentrations after 21 hours, all experimental animals are alive.

In 0.01% concentration, all daphnia are still convulsing at lower quarter of jar. Heartbeat rate and respiratory movements are very low, the intestine is partly refilled but loosely packed.

In 0.005% concentration, the same symptoms were noted as above.

In 0.002% concentration, heartbeat rate and respiratory movements are moderately depressed, the intestine is partly filled, the animals swim normally.

In 0.001% concentration, animals appear normal.

Response of Daphnia Magna to Paredrine Hydrobromide

Concentrations: 0.1%, 0.01%, 0.005%, 0.002%, 0.001%

Seven animals in museum jars containing 100 cc. of each concentration.

0.1% concentration in culture water

After 12 min. Mild excitation, 6 out of 7 animals are coming to surface.

After 17 min. All up at surface, excitation is passing into convulsions, heartbeat is up and respiratory movements are fast.

After 25 min. Convulsions are very obvious.

After 60 min. Heartbeat is depressed to 180/min., respiratory movements are depressed moderately, evacuation is 50-100%, the eye is unaffected.

After 21 hours. All are alive on bottom, 6 convulsing, 1 in coma. Heartbeat rate is very much depressed, respiratory movements are spasmodic and feeble, the eye is unaffected, the intestine partly refilled.

Lower concentrations: 0.01%, 0.005%, 0.002%, 0.001%: Within 4 hours.

From 20 min. on. Animals swim lethargically in straight line up and down, no convulsions.

Up to 60 min. No convulsions. After that 1 animal in 0.01% is reacting with convulsions and depressed heartbeat rate.

After 3 hours. No reactions are visible.

0.01% concentration: After 21-22 hours.

Daphnia tend to swim in lower quarter, swimming excitedly with jerky motions and with frequent headlong collisions with bottom. One animal with heartbeat rate of 120/min. respiratory movements depressed, 100% evacuation; another with heartbeat rate of 170/min., respiratory movements only slightly depressed, intestine partially evacuated. Remaining 5 daphnia with normal appearance except for swimming behavior.

0.005% concentration: After 21-22 hours.

Daphnia exhibit same swimming behavior as in 0.01% concentration. Otherwise normal behavior with release of young is taking place.

0.002% concentration: After 21-22 hours.

Daphnia exhibit a similar but less marked swimming behavior than those in 0.01% and 0.005%. Release of young was observed.

0.001% concentration: After 21-22 hours.

No visible effects.

Response of Daphnia Magna to Paredrinol SO_4

Concentrations: 0.1%, 0.01%, 0.005%, 0.002%, 0.001%

Seven daphnia were placed in museum jars containing 100 cc. of each concentrations.

0.1% concentration in culture water

After 8 min. Drug effect is apparent; 3 animals convulsing at surface, others excited.

COMPARATIVE PHYSIOLOGICAL ACTION ON DAPHNIA MAGNA

BENZEDRINE SULFATE

Conc.	Method of Application	Muscular System	Time	Digestive System	Time	Respiratory System	Time	Cardiac System	Time	Glandular System	Time	Nervous System	Time
0.1%	Comparoscope chamber (10 cc.) 5 daphnia	Convulsions surface swimming	3 min.	Constriction	3 min.	Depressed	3 min.	Depressed 100/min.	3 min.	—	—	Eye relaxed	3 min.
		Convulsions weaker	10 min.	Partial evacuation	50 min.	Slow, feeble	50 min.	Normal (280-300)	50 min.	—	—	Same	50 min.
0.1%	Vie-tubes 5 daphnia			Laxative effect small, A. O. A. C. method	20-25 min.								
0.01%	Vie-tubes 5 daphnia			1-50% 2-75% 2-100%	20-25 min.								
0.01%	Museum jars 100 cc. 10 daphnia	Convulsions	7 min.	100%	47 min.	Slow	47 min.	150-180/ min.	47 min.	—	—	—	—
		"	3 hrs.										
0.005%	"	"	13 min.	—	—	Slightly depressed	13 min.	200/min.	13 min.	—	—	—	—
		"	2 hrs.	100%	2 hrs.	Further depressed	2 hrs.	160/min.	2 hrs.	—	—	—	—
0.002%	"	—	3 hrs.	75-100%	3 hrs.	Slightly depressed	3 hrs.	250/min.	3 hrs.	—	—	—	—
0.001%	"	—	21 hrs.	5-50%	3 hrs.	—	—	—	—	—	—	—	—

PAREDRINE HYDROBROMIDE

0.1%	Museum jars 100 cc. 7 daphnia	Mild excit. Early convul. Convulsions	12 min. 17 min. 25 min.	Evacuation 50-100%	1 hr.	moderately depressed	1 hr.	180/min.	1 hr.	—	—	—	—
0.01%	"	Lethargic swimming Animal convulsed	20 min. 1 hr.	100% (1 daphnia)	21-22 hrs.	" (1 daphnia)	21-22 hrs.	170/min. 120/min. (2 daphnia)	21-22 hrs.	Release of young	21-22 hrs.	—	—
0.005%	"	—	—	—	—	—	—	—	—	Same	21-22 hrs.	—	—
0.002%	"	—	—	—	—	—	—	—	—	Same	21-22 hrs.	—	—
0.001%	"	—	—	—	—	—	—	—	—	—	—	—	—

PAREDRINOL SULFATE

0.1%	Museum jars 100 cc. 7 daphnia	Convulsions	8 min.	—	—	About normal	18 min.	200/min.	18 min.	—	—	—	—
						Depressed	2½ hrs.	150-180/ min.	2½ hrs.	—	—	—	—
0.01%	"	Mild excit. More marked	24 min. 34-45 min.	—	—	Normal	1 hr.	Normal	1 hr.	—	—	—	—
0.005%	"	Mild excit. Excited swimming in lowest quarter	42 min.	—	—	—	—	—	—	—	—	—	—
			22-23 hrs.	—	—	Depressed	22-23 hrs.	Depressed	22-23 hrs.	—	—	—	—
0.002%	"	Slight excitation	22-23 hrs.	—	—	—	—	—	—	—	—	—	—
0.001%	"	Slight excitation	22-23 hrs.	—	—	—	—	—	—	—	—	—	—

IOLOGICAL ACTION ON DAPHNIA MAGNA

BENZEDRINE SULFATE

ry	Time	Cardiac System	Time	Glandular System	Time	Nervous System	Time	Toxicity	Time
l	3 min.	Depressed	3 min.	—	—	Eye relaxed	3 min.	Recovery in culture H_2O after 1 hour exposure	Complete next day
le	50 min.	100/min. Normal (280-300)	50 min.	—	—	Same	50 min.	15 dead, museum jar	21 hours
	47 min.	150-180/min.	47 min.	—	—	—	—	Alive, convulsions, debility	21 hours
	13 min.	200/min.	13 min.	—	—	—	—	Alive, convulsions, debility	21 hours
	2 hrs.	160/min.	2 hrs.	—	—	—	—		
	3 hrs.	250/min.	3 hrs.	—	—	—	—	Alive, slight depression	21 hours
	—	—	—	—	—	—	—	Normal	21 hours

AREDRINE HYDROBROMIDE

y	1 hr.	180/min.	1 hr.	—	—	—	—	Alive, debility, convulsions	21-22 hrs.
a)	21-22 hrs.	170/min. 120/min. (2 daphnia)	21-22 hrs.	Release of young	21-22 hrs.	—	—	Alive, 5 daphnia excited, swimming	21-22 hrs.
	—	—	—	Same	21-22 hrs.	—	—	Same, less marked	21-22 hrs.
	—	—	—	Same	21-22 hrs.	—	—	"	21-22 hrs.
	—	—	—	—	—	—	—	—	—

PAREDRINOL SULFATE

	18 min.	200/min.	18 min.	—	—	—	—	5 dead, 2 advanced debility	22-23 hrs.
l	2½ hrs.	150-180/min.	2½ hrs.	—	—	—	—		
	1 hr.	Normal	1 hr.	—	—	—	—	Alive, debility, convulsions	22-23 hrs.
	—	—	—	—	—	—	—	Alive	22-23 hrs.
l	22-23 hrs.	Depressed	22-23 hrs.	—	—	—	—	"	"
	—	—	—	—	—	—	—	Alive	22-23 hrs.
	—	—	—	—	—	—	—	Alive	22-23 hrs.

After 18 min. Heartbeat rate is 200/min., respiratory movements are fast, convulsive swimming is noted; 6 daphnia at surface, one at bottom.

After 1 hour. No apparent change in internal junction.

After 2½ hrs. Heartbeat rate is 150-180/min., respiratory movements depressed, convulsive swimming occurs, with animals at bottom of jar.

After 22-23 hrs. Five dead, 2 alive with advanced debility.

0.01% concentration in culture water

After 24 min. Mild excitation in swimming. Otherwise no other apparent symptoms.

After 35-45 min. Excitation more marked.

After 1 hour. Heartbeat rate normal, respiratory movements fast.

After 2½ hours. No change.

After 22-23 hours. All at bottom convulsing. Heartbeat rate and respiratory movements are depressed.

0.005% concentration in culture water

After 42 min. Mild excitation.

After 22-23 hours. Marked excitation, heartbeat rate and respiratory movements are depressed. Animals swim in lowest quarter.

.002% and .001% concentrations in culture water

After 1 hour. No visible effects.

After 2½ hours. Same.

After 22-23 hours. Slight excitation in swimming movements which are different from normal. Otherwise no internal changes visible.

Conclusions

From tests made on *Daphnia magna,* the following criteria were used to evaluate the activity of benzedrine sulfate and derivatives: the speed of the onset of convulsive locomotion depression of respir-

atory and cardiac systems and death at similar concentrations. Judged by these responses to solutions of comparative percentage concentrations Benzedrine sulfate is considered more active physiologically than Paredrinol sulfate or Paredrine hydrobromide, while Paredrinol sulfate is rated more active physiologically than Paredrine hydrobromide.

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STUDIES OF LECITHIN SOAP II

"Effect of Lecithin Soap upon Vitamin 'A'"

By Saul Caspe and L. G. Hadjopoulos

THE effect and application of soap as a cleansing agent, emulsifier and lubricant has been known for many years. The introduction of new types of soap marketed in novel forms is a manifestation of the growth of the soap industry. The knowledge of the detergent properties of soap has been prolifically accumulated during the 19th and 20th centuries and the research carried out during this period has elucidated the mechanism of this phenomenon. It can be safely stated today that the amount of soap consumed is a reliable index of a country's civilization. The growth of large scale laundry enterprises, glycerine by-product rectification plants and numerous other industrial plants is closely allied to the industrial manufacture of soap.

Intensive study of the properties of various soaps has revealed, in rather recent times, that certain soaps possess a marked bactericidal property. The medical use of soap as suppositories, and for colonic irrigation and lubrication, but more importantly, as an intestinal bactericide when taken per os is predicated upon these recent findings. Although the medicinal applications of soap as an external and internal tissue bactericide, as a disinfectant, sclerosing agent, etc., are small in comparison to its use as a general universal cleanser, the extension of its values in other fields has increased its world market and our knowledge.

Our previous investigation disclosed the fact that lecithin soap is superior to other known standard soaps as an intestinal bactericide and detoxifying agent. The present investigation was pursued to determine whether lecithin soap possesses properties similar to its parent substance, lecithin in preserving vitamin "A".

H. Bollman (1) improved the durability of refined vegetable oils by the addition of lecithin. Recently several studies (2, 4) have been made in respect to the value of lecithin as an antioxidant. The work of Holmes, Corbet and Hartzler (3) indicates a useful experimental method and data concerning the destruction of vitamin "A" in Halibut Liver Oil under oxygen at 96 degrees C. and the retarded destruction of the same in the presence of 1 per cent.-5 per cent. lecithin.

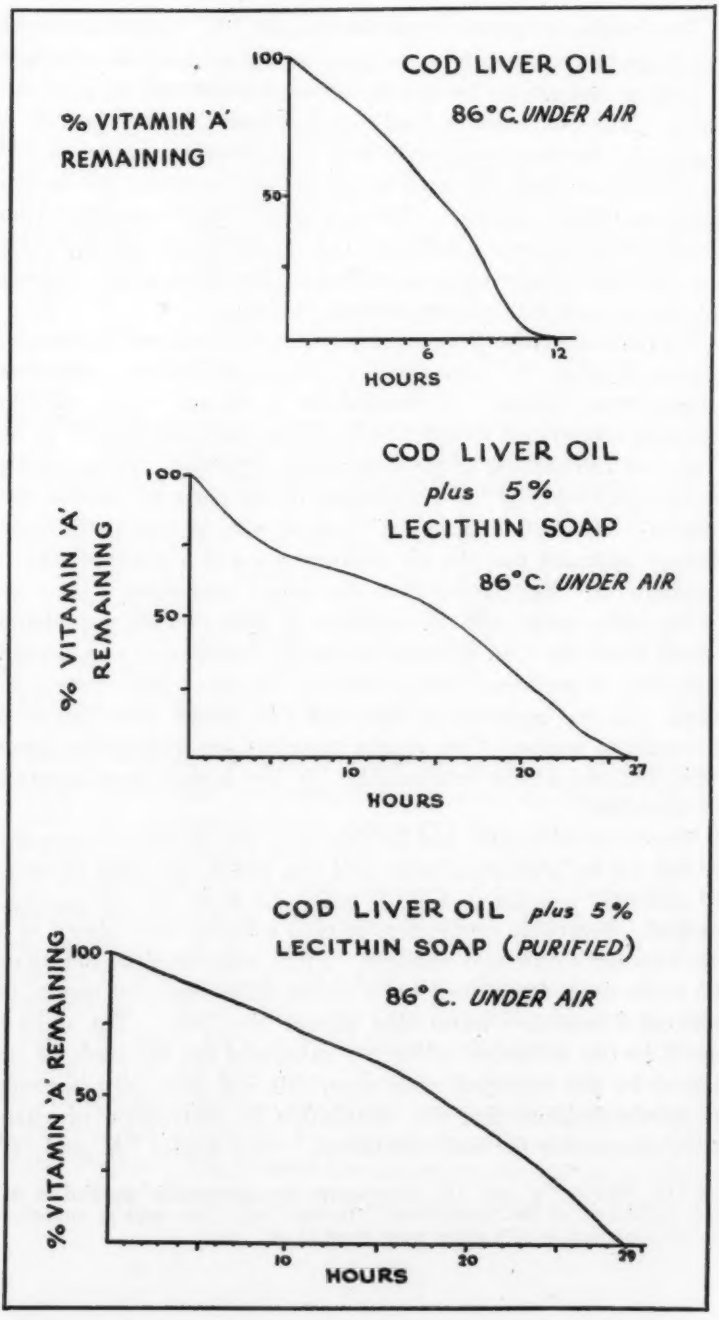
Our lecithin soap was prepared by melting 100 grams of lecithin in a pyrex beaker on a water bath. The melted lecithin was poured into approximately 40 cc. of 50 per cent. aqueous sodium hydroxide to which was added 5 cc. of ethyl alcohol and a few drops of alcoholic phenolphthalein to prevent foaming and indicate the extent of alkalinity. The reaction mixture is continuously stirred and heated on water bath for one hour. At the conclusion some dilute acetic acid, 150 cc. of hot water and 100 grams of sodium chloride are respectively added. The mixture is transferred to a separatory funnel where the salted-out soap is washed free of salt and excess alkali with ice cold water.

This lecithin soap is then purified by resaponification with an alcoholic sodium hydroxide solution; the containing flask is heated on steam bath under reflux condensor for one hour. The alcoholic soap solution is then diluted with hot water and salted out with sodium chloride and the salted-out soap is washed thoroughly with ice cold water. The soap is then dissolved in warm 95 per cent. ethyl alcohol, filtered and fractionally crystallized. By analysis the soap was found to contain both nitrogen and phosphorus.[1]

Our experiments were divided into three parts. The first part was to determine the effect of lecithin soap upon heat and air destruction of vitamin "A" in cod liver oil. The second part was to determine the preserving effect of lecithin soap upon vitamin "A" concentrate in oil solution on long standing. The third part was to determine the preserving effect of lecithin soap upon vitamin "A" concentrate in water emulsion on long standing.

Three Woulff bottles equipped with thermometers and with outlet tubes connected to vacuum pump (slight vacuum maintained to keep air in circulation above the surface of oils) to keep air in circulation through the bottles were placed into water baths and maintained at a temperature of 86° C. Into the first was poured 20 cc. of standard cod liver oil guaranteed to contain not less than 600 vitamin "A" units per gram of oil; into the second was poured 20 cc. of the same cod liver oil into which 5 per cent. of lecithin soap was dissolved; into the third was poured 20 cc. of the same cod liver oil into which 5 per cent. of the purified lecithin soap was dissolved. Although the three tests were run concurrently, they were run as separate entities. There are no connecting tubes between the bottles. The graphs of the retarded destruction of vitamin "A" are given on the following page.

[1] We are thankful to Mr. S. Liberman of the College of Pharmacy, Columbia University, New York City, for some of the analysis of lecithin soap.


COD LIVER OIL
86°C. UNDER AIR
% VITAMIN 'A' REMAINING
100
50
6
12
HOURS
COD LIVER OIL
plus 5%
LECITHIN SOAP
86°C. UNDER AIR
% VITAMIN 'A' REMAINING
100
50
10
20
27
HOURS
COD LIVER OIL plus 5%
LECITHIN SOAP (PURIFIED)
86°C. UNDER AIR
% VITAMIN 'A' REMAINING
100
50
10
20
29
HOURS

The graphs are plotted from the vitamin "A" content determined every three hours by withdrawing 0.5 cc. of cod liver oil or solution and making estimations by use of antimony trichloride in chloroform solution. The blue color is read in a Lovibond Tintometer. As the vitamin "A" becomes completely destroyed, readings are taken every hour in order to limit the error in actual time consumed for complete destruction within one hour. The first graph represents three 3-hour and two 1-hour interval readings. The second graph represents eight 3-hour and two 1-hour interval readings. The third graph represents eight 3-hour and four 1-hour interval readings.

Further comparisons were made of lecithin and lecithin soap with respect to vitamin "A" preservation. In our preliminary experiments we noted that vitamin "A" concentrate in oil and water emulsions underwent accelerated destruction by increasing such factors as light and air. A comparison of the destruction of vitamin "A" in oil solution (one part vitamin "A" concentrate in 100 parts oil) and in water emulsion (one part vitamin "A" concentrate in 100 parts water) definitely indicated that the oil solutions showed a much slower rate of vitamin "A" destruction than the water emulsions. They were kept in similar tubes and the exposure to light and air was identical for both solutions. An attempt was made therefore to conduct these comparative experiments with a definite degree of uniformity. It is obvious that the intensity of light and heat varies from day to day and season to season. Our results therefore are quantitative insofar as they indicate a ratio relationship. A few typical experiments are here described.

One gram of lecithin and lecithin soap was dissolved respectively into two 100 cc. portions of oleic acid into which one gram of vitamin "A" and "D" concentrate [2] made from cod liver oil was previously dissolved. Ten cubic centimeters of each solution were placed in test tubes exposed to air and sunlight. From time to time, the vitamin "A" units were determined on a comparative basis by means of a Lovibond Tintometer using blue glasses No. 1180. The units expressed in the following tables are calculated on the basis of units obtained by the biological tests upon this cod liver oil concentrate. The results indicate that the retardation in destruction of vitamin "A" is comparable for both substances. (See Tables "A" and "B".)

[2] The vitamin "A" and "D" concentrate was generously supplied to us by Dr. J. K. Marcus of the International Vitamin Corp. The units of vitamin "A" and "D" contained in each gram were given to us.

TABLE "A"

COMPARISON OF LECITHIN, LECITHIN SOAP AND OLEIC ACID AS PRESERVATIVES OF VITAMIN "A" (IN "A" AND "D" CONCENTRATE)

Vitamin "A" Concentrate in Oleic Acid 1 : 100:

Time	Lecithin 1 : 100	Lecithin Soap 1 :100	Control
12/28/36	2680*	2900*	3000*
1/14/37	2680	3000	2570
2/14/37	1498	1395	0
2/27/37	342	342	0
7/26/37	342	342	0

TABLE "B"

COMPARISON OF LECITHIN, LECITHIN SOAP AND PEANUT OIL AS PRESERVATIVES OF VITAMIN "A" (IN "A" AND "D" CONCENTRATE)

Effect of 65° C. heat aeration for 2 hrs. and subsequent exposure to light and air

Vitamin "A" Concentrate in Peanut Oil 1 : 100:

Time	Lecithin 1 : 100	Lecithin Soap 1 :100	Control
1/9/37	2896	2900	2980
2/20/37	428	445	222

*Vitamin "A" units per gram oil.

In the third part of this experimental work, it was desirable to determine the vitamin "A" preservation in water emulsions. Vitamin "A" and "D" concentrate made from cod liver oil was diluted ten times (10X) with diethylene glycol. To each of three test tubes containing respectively 9 cc. of approximately 1 per cent. lecithin soap in aqueous solution; 9 cc. of lecithin in water, and 9 cc. diethylene glycol was added 1 cc. of vitamin "A" and "D" concentrate in diethylene glycol (1 :10). These test tubes were allowed to stand in sunlight in contact with air, and from time to time samples were taken for dry spot plate tests with antimony trichloride in ($CHCL_3$) chloroform. The dry spot plate tests are conducted as follows: Two drops of the water emulsion are placed in a groove on spot plate and then the spot splate is placed in a dessicator under nitrogen or carbon dioxide. Within a few minutes the drops dry out leaving a dry spot which can then be tested by adding antimony trichloride to it.

It was apparent from these preliminary tests that lecithin soap was superior to lecithin in retarding the destruction of vitamin "A" enhanced by oxidation, sunlight and the presence of water. The lecithin soap emulsifies with water whereas the lecithin is not readily emulsifiable. The vitamin "A" was extracted from these water emulsions by peroxide-free ether under anaerobic conditions, and the lipoid residue is subsequently dissolved in chloroform. The vitamin "A" units are determined by reading the color intensity produced by antimony trichloride in a Lovibond Tintometer. A typical result of several duplicated studies is tabulated below:

LECITHIN SOAP AS PRESERVATIVE OF VITAMIN "A" ("A" and "D" CONCENTRATE) IN WATER EMULSION

Vitamin "A" Concentrate in:

Time	Diethylene glycol Solution 1 : 100	Lecithin Soap 1 : 100 Water Emulsion Solution 1 : 100	Control Water Emulsion Solution 1 : 100
10/1/37	3000	2900	2900
10/12/37	2500	2600	1500
10/24/37	1500	1550	300
11/4/37	590	590	0

Conclusions

1. Five per cent. of lecithin soap retards the heat and air destruction of vitamin "A" in cod liver oil.

2. Lecithin soap in concentrations as low as 1.0 per cent. retard destruction of vitamin "A" in oil solution and water emulsion.

3. Water emulsions of vitamin "A" and "D" concentrates from cod liver oil show an accellerated destruction of vitamin "A" in comparison to oil solutions.

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GROWING PLANTS WITH CHEMICAL SOLUTIONS

By R. Crawford and R. E. Crawford

OUR studies on the growth of plants nourished by solutions of chemicals were carried on out of doors during the summer of 1938. As in our previous work (1) tomatoes were chosen as the experimental plants and Wanamassa, N. J., remained the site of operations.

Briefly the method of procedure was as follows. Containers, with provision for thorough drainage, were filled with an inert loose aggregate in which the roots of the plants were placed in the same manner as they would have been placed had soil been used. This aggregate was saturated daily with a solution which contained all the chemicals necessary to the growth of the plants. Tomato plants, which had been grown from seed sown in the soil in cold frames, were taken up, freed of as much of the soil clinging to their roots as possible, and placed in sets of three in wooden boxes two feet long, one foot wide, and one foot deep. These boxes were then placed under a trellis made of galvanized iron wire strung on two by four inch posts nine feet high. While the shape of the land available for this work forced us to run this trellis in an East and West direction about eight feet south of a row of trees and tall bushes the plants did have a good exposure to the South and received direct sunlight from about nine o'clock in the morning until four in the afternoon.

In order to test the relative merits of beach sand and sifted coal ashes; the portion of the ashes which passed through quarter inch mesh wire and remained on wire mosquito netting was used; four of the boxes were filled with ashes and two with sand. The same solution was used in all six boxes at all times. Although the difference was not great enough to be really significant or conclusive the plants in the ashes seemed to grow and produce slightly better than those in the sand.

The solution known as formula number 3 in our first paper (1) was used from the beginning of this experiment on May 12th until June 15th. By this time it was evident that this solution was not producing the desired amount of growth.

The composition of formula number 3 is as follows.

Sodium nitrate	1.76 Gm.
Superphosphate	1.72 Gm.
Epsom Salt	4.20 Gm.
Potassium Chloride	1.17 Gm.
Iron Chloride	0.01 Gm.
Water	1 gal.

Knowledge of the fact that nitrate of soda would produce a rapid increase in the rate of growth of plants growing in the ground, naturally suggested the doubling of the amount of nitrate in this solution. After several days' trial it was evident that this also was failing to produce the desired results so the nitrate was returned to its former value.

A dramatic increase in the rate of growth and fruit production followed the addition, late in June, of 0.04 Gm. of iron chloride, manganese chloride, zinc chloride, copper sulfate and boric acid to each gallon of the solution. The importance of the so-called trace elements, iron, manganese, zinc, boron and copper, is stressed by the literature. (2), (3) Further changes in the quantities of these trace elements did not produce further improvement, so they have been left at this level.

The composition of this improved solution, which for the sake of continuity with our previous work we will call formula number 4, follows.

Sodium Nitrate	1.76 Gm.
Superphosphate	1.72 Gm.
Epsom Salt	4.20 Gm.
Potassium Chloride	1.17 Gm.
Iron Chloride	0.04 Gm.
Manganese Chloride	0.04 Gm.
Zinc Chloride	0.04 Gm.
Copper Sulfate	0.04 Gm.
Boric Acid	0.04 Gm.
Water	1 gal.

Due to the fact that the solution used during the first part of the summer was not perfected and partly perhaps to the fact that the situation of these plants was not ideal the yield was disappointing.

One hundred ten and a half pounds of fruit were picked from these vines which grew over the top of the trellis.

A study of the growth of seedlings by this method was begun on August 7th. Tomato seeds were sown in shallow drills in sand. The sand was kept moist with a solution made by diluting formula number 4 to one-fifth its usual strength. The seeds sprouted and the young plants appeared above the surface of the sand in six days.

As soon as the young plants appeared the use of diluted solution was discontinued and full strength formula number 4 was used. The seedlings grew rapidly and were ready for transplanting in a week after they first appeared.

Transplanting proved to be an easy task. Running the finger beneath the row of seedlings loosened the sand so that the plants could be lifted out without injury to their roots. The roots of the plants were placed in holes punched in fresh sand. This sand was pushed in around the roots and saturated with solution number 4.

The growth continued satisfactorily and on September 4th the plants were transplanted to pots. The transfer was accomplished by picking up, in the fingers, a clump or ball of the sand with the roots of the plant intact in it and placing it in a three-inch flower pot, which was then filled with sand. Watering was accomplished by immersing the pot to its rim in the solution until the sand was saturated and then withdrawing the pot and allowing the excess solution to drain out.

On October 1st these tomatoes, fine healthy stocky plants eleven inches high, and each bearing a clump of buds, were transfered to the tanks in our greenhouse. They will be used in further investigations this winter.

The successful completion of these three transplantings without the loss of any plants points out one of the advantages of this method of raising seedlings. Transfer of seedlings, grown in sand, without injury to their roots is facilitated by the looseness of the medium. The usual critical period of a day or two following transplanting while the plants are extending roots into the new environment in search of nourishment is largely eliminated by supplying the needed nourishment in readily available form in solution.

Damping off, a fungous disease that frequently takes heavy toll of young seedlings did not cause trouble at any time during the growth of these seedlings. This would seem to indicate either that the sand

was relatively free of the organism causing the disease or that the better aeration provided by the sand discourages its growth.

Two excessively wet spells during the summer, July 17th-24th and the hurricane of September 21st, caused the tomato growers of Monmouth county heavy losses in decayed fruit and drowned vines. During these wet periods the drains on the boxes were left open allowing the excess moisture to escape. By this means the losses from these experimental vines were confined to one decayed tomato during the first wet spell and one tomato blown from the vines by the hurricane.

At all times during the summer the quality of the fruit raised by this method was at least equal to that raised in the field. For a few days following each of the storms mentioned above the fruit raised by this method were far superior in quality because they did not become watery as did those raised in the field.

The writers hope that the publication of this paper will help and encourage others to enter this fascinating field and have a share in its development.

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SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

Hay fever is a sneezy, pollen allergy, of much discomfort to the victim, yet lightly regarded by those who have never experienced its cantankerous symptoms.

A successful treatment of hay fever with potassium salts is given a preliminary report by Dr. Benson Bloom, of Tucson, Ariz. (*Journal, American Medical Association,* Dec. 17.)

Striking benefit was obtained by twenty-nine patients given potassium chloride, Dr. Bloom reports.

The method is simple and no complications or "side effects" were noted, although further studies are indicated, he declares.

These salts also were successfully used by Dr. Bloom in treating several cases of urticaria (hives), eczema, nasal polyposis, chronic allergic sinusitis and migraine.

In cases of chronic asthma the same treatment helped not at all.

The crude cruelty of the totalitarian governments receives more confirmation in news recently received from Austria. From the University of Vienna, once a place where liberality and freedom of thought paraded, and whose faculty was world renowned, comes the news that half of the medical faculty is all that is left since the Nazi purge excluded the non-Aryans.

The men who were summarily dismissed from their life-long services are men known the world over for their contributions to the medical sciences. And time alone will tell—as it has always told, how damaging is such intolerance.

Smoking cigarettes raises the blood pressure in both normal persons and in patients suffering with high blood pressure, Drs. E. A. Hines, Jr., and Grace M. Roth of the Mayo Clinic found in a study of eighty-six persons.

The effect of tobacco smoking on blood pressure is not due entirely to the action of a stimulus on specially sensitive blood vessel systems. Part of the effect, at least, is the result of some element in the tobacco smoke which causes constriction of the blood vessels. This element in the tobacco smoke was not identified in the report made by the two scientists at a recent staff meeting of the Clinic.

The rise in blood pressure following smoking was greater in high blood pressure patients than in normal persons except in the case of high blood pressure patients who had never smoked before. This latter difference is attributed to the fact that inexperienced smokers do not inhale as much smoke as regular smokers.

And still the avertisers say, "Be nonchalant."

Colchicine, long an ingredient in rheumatism remedies, has found new employment in horticulture. It greatly affects plant growth. But plant cells can be induced to double their chromosome numbers and thereby produce giant offspring and other sudden evolutionary changes by another chemical besides colchicine, with which these changes were first induced by scientists of the Carnegie Institution of Washington. The new compound is known as acenaphthene, and it has been used in Russia by Dr. Dontcho Kostoff of the Academy of Sciences of the USSR.

The compound is not applied in solution, like colchicine, Dr. Kostoff reports. (Nature, Oct. 22) The plants are exposed in closed spaces to the effects of its vapor as it comes off from crystals by the process of sublimation or dry evaporation.

Toad and snake venom have long been used by Chinese in their queer materia medica. And here seems to be some justification for such use.

Relief of the severe pain of cancer, tic douloureux, locomotor ataxia and a number of other conditions without any dulling or depressing effect on the mind, but, on the contrary, with a stimulation of intellectual processes—these are the effects chalked to the credit of cobra venom in a report by Dr. David I. Macht and his son, Moses B. Macht, of the pharmacological research laboratory of Hynson, Westcott and Dunning at Baltimore.

Although cobra venom is a poison, the Baltimore scientists report that it can be safely given in sterile solution in suitable doses.

In the new and colorful antiseptic mercurochrome, the highly toxic qualities of mercury and its poor rate of dispersion, due to local coagulation, are compensated for by fluorescein, a dyestuff of high penetration and low toxicity. By the way the latest manifestation of mercurochrome is in the new germ-proof, kiss-proof and soup-proof mercurochrome lip salve.

A similar combination of iodine with fluorescein is already available under the name of iodeosine (tetra-iodo-fluorescein $C_{20}H_8I_4O_5$). It has been used as an indicator, and possesses a color degree of dizzy red, not quite as spectacular however, as that of mercurochrome. So far as I know it has never been suggested as an antiseptic. It is unfortunately insoluble in water, although freely soluble in alcohol. A water-soluble sodium salt of this compound is known as erythrosine, and is a permissible coal tar color for camouflaging food. For all we know then, the bright red pop soda water of circus days may make a better gargle than a beverage.

The thyroid gland is present in all vertebrate animals beginning low down in the scale, with the lampreys and complicating its structure and increasing its size as it occurs farther up in the evolutionary scale. In fish the thyroid occurs as small scrubby patches little larger than pin heads—scattered along the important blood vessels. Then in the reptiles it is a little larger and more compact, and still more prominent among the birds and the mammalia. But it is in the primates and in man that it attains to greatest size. Thus it might be said that the thyroid gland is an indicator of evolution.

The farther we are from our early home in the sea the larger the thyroid gland. Now if evolution continues along the same line—a million years from now our thyroid may have become the most important organ in our bodies. And man's appearance may be consequently so changed that instead of being the good-looking creature he thinks he now is—he will have evolved into a pop-eyed, fat-headed, chinless creature—the space between his chin and his collar button having been taken over by his constantly expanding iodine plant.

But that is too far off to worry about. Several things may happen in a million years.

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

An Introduction to Microchemical Methods. By Cecil L. Wilson, M. Sc., Ph. D., The Queens University of Belfast. Published by the Chemical Publishing Co. of New York, Inc. With diagrams. Price, $3.00.

With the publication, in 1923, of the first number of the JOURNAL, Mikrochemie, Microchemistry may be said to have taken its place as a recognized science. The increasing number of publications, both in journals and in the form of handbooks, indicates that a knowledge of microchemical methods is now essential to every practising chemist.

This text is designed to acquaint the student with the vast field covered by microchemistry, and to give him a basic working knowledge of microchemical methods of analysis, both qualitative and quantitative, organic and inorganic. The author presumes that the study of this text has been preceded by three years of scientific training and yet he devotes a large portion of this small volume to a consideration of the design and structure of optical apparatus with the result that the actual operations and functions of microchemical methods have been slighted. The application to this field of chemistry of the compound microscope, the polarizing microscope, the colorimeter, nephelometer, tintometer, and the spectrograph are indicated.

The technique of crystallizing material in microscopic quantities is explained and specific crystal tests are given, as are spot tests for the qualitative identification of many anions and cations. The author also diagrams a systematic scheme of analysis for detecting the presence of some of the commoner cations and for a number of anions. This is merely a base and acid chart whose methods have been modified for the separation and identification of small amounts of materials in mixtures.

Gravimetric and volumetric methods are described for the quantitative determination of a few inorganic substances and although the author tells us about organic operations he skips lightly over the surface of organic quantitative analysis. The book is concluded with a sketchy indication of the use of photomicrography in microchemical methods of analysis. The appendix contains a list of reagents and

test papers used in the qualitative determinations as described in the text.

Taken all in all, the author has devoted entirely too much space in this small volume to a consideration of subjects which, as he explains, should have preceded an introductory course in microchemical methods of analysis.

F. W. SCHILLER.

The American Illustrated Medical Dictionary; Dorland: A complete dictionary of the terms used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, Nursing, Veterinary Science, Biology, Medical Biography, etc., with the pronunciations, derivations, and definitions. By W. A. Newman Dorland, with the collaboration of E. C. L. Miller. Eighteenth edition. 1607 pages; 942 illustrations. W. B. Saunders Company, Philadelphia, 1938.

The present edition of this well-known dictionary, which is generally regarded by the American medical profession as the most satisfactory, has been revised and augmented by the addition of 5000 newly-defined words. In order to bring the dictionary up to date, the authors have directed their attention to the fields of endocrinology, immunology, pathology, medical chemistry, and clinical medicine, where the greatest number of revisions and additions appear. More than 100 new tests are described. Included also are tables of arteries, veins, muscles, nerves, dosage, etc., which, supplemented with an inclusive list of new drugs, medicinal chemicals, their formulas, serums, vaccines, treatments, operations, exanthemata, etc., make this dictionary a medical encyclopedia.

By conforming to the adopted standards of the American Medical Association, Society of American Bacteriologists, American Chemical Society and other scientific bodies, the terminology represents that approved by the best qualified authorities. Of historical interest are the brief biographies of outstanding investigators whose names have been given to diseases and treatments. A distinctive feature of this edition is the gallery of 283 portraits of past leaders in the field of medicine. This valuable reference book will be an indispensable addition to any ready reference library.

R. L. MCNEIL, JR.

Vitamins and Hormones. Volume I. By Drs. Hellmut Brederick and Robert Mittag, second revised edition in German. 138 pages. Published by Hirzel, Leipzig. Price, Reich marks 7.00.

The little volume, just published, deals briefly with the results of research on vitamins and hormones. Subsequent volumes, in progress of preparation for several years, will give information concerning their technical preparation.

It is the avowed aim of Dr. Carlsohn (editor of the Series of "Chemistry and Technic of Our Time"), to have the subject matter of the 4-volume work on vitamins and hormons discussed in such detail as to interest and benefit the research worker as well as his technical assistant, and to serve as a guide to physicians and pharmacists alike.

The scope of Volume I is indicated in an elaborate outline, permitting quick orientation. The discussion includes such recent vitamins as H, J, K and P. It records the status of hormon studies of both animals and plants, either emphasizing the chemical nature of these substances, or stating the lack of knowledge, where such prevails.

As an interpretative survey the brevity of the discussion is an asset. As a bibliographic record, in spite of 427 references, this brevity is disappointing. Thus the work on such important hormonal substances as the intestinal cholecystokinin, (apparently the only gall-bladder evacuant thus far known), is altogether omitted.

However, the book will serve its purpose well and probably prove even more popular than the first edition published 1936, especially as two additional volumes for the preparation of these essential life substances have now also become available.

ARNO VIEHOEVER.

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